

Reumatismo - The Italian Journal of Rheumatology

<https://www.reumatismo.org/reuma>

eISSN 2239-7132

Publisher's Disclaimer. E-publishing ahead of print is increasingly important for the rapid dissemination of science. The Early Access service lets users access peer-reviewed articles well before print/regular issue publication, significantly reducing the time it takes for critical findings to reach the research community.

These articles are searchable and citable by their DOI (Digital Object Identifier).

Reumatismo is, therefore, E-publishing PDF files of an early version of manuscripts that have undergone a regular peer review and have been accepted for publication, but have not been through the copyediting, typesetting, pagination, and proofreading processes, which may lead to differences between this version and the final one.

The final version of the manuscript will then appear in a regular issue of the journal.

The E-publishing of this PDF file has been approved by the authors.

Please cite this article as:

Castro de Oliveira Figueirôa MdL, Moura Costa MC, Rocha Lobo P, et al. **Acute heart failure due to myocarditis in Takayasu's arteritis.** *Reumatismo* doi: 10.4081/reumatismo.2024.1681

Submitted: 08-11-2023

Accepted: 16-04-2024

 © the Author(s), 2024
Licensee PAGEPress, Italy

Note: The publisher is not responsible for the content or functionality of any supporting information supplied by the authors. Any queries should be directed to the corresponding author for the article.
All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

Acute heart failure due to myocarditis in Takayasu's arteritis

M.d.L. Castro de Oliveira Figueirôa^{1,2}, M.C. Moura Costa²,
P. Rocha Lobo², A.L. Souza Pedreira¹, M. Barreto Santiago^{2,3}

¹BAHIANA - School of Medicine and Public Health, Salvador, Brazil; ²Professor Edgard Santos University Hospital, Federal University of Bahia, Salvador, Brazil; ³Specialized Rheumatology Services in Bahia (SER), Salvador, Brazil

Corresponding author: Maria de Lourdes Castro de Oliveira Figueirôa, BAHIANA - School of Medicine and Public Health, Av. Dom João VI, 275 - Brotas, Salvador, Brazil.

Phone: (71) 3276-8200

E-mail: mariafigueiroa3030@gmail.com

Key words: Takayasu's arteritis, heart failure, myocarditis.

Contributions: all the authors made a substantial intellectual contribution, read and approved the final version of the manuscript, and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors declare no potential conflict of interest.

Ethics approval and consent to participate: not applicable.

Patient consent for publication: the patient's legal guardian's consent was given to share this case for scientific purposes.

Funding: none.

Availability of data and materials: data and materials are available by the authors.

Summary

Takayasu's arteritis (TA) is a granulomatous vasculitis that involves the aortic artery and its branches, resulting in stenosis, occlusion, and aneurysmal dilatation. Cardiovascular involvement is one of the main complications and a major cause of mortality in these patients. Herein, we describe the case of a woman with TA who presented with severe acute heart failure secondary to myocarditis and responded well to immunosuppressive therapy.

Introduction

Takayasu's arteritis (TA) is a granulomatous vasculitis that involves the aorta and its branches and may result in stenosis, occlusion, and aneurysmal dilatations (1-3). It preferentially affects women of reproductive age, and its clinical manifestations include systemic symptoms and specific signs of vascular involvement, such as limb claudication, abdominal murmur, and focal central nervous system deficits due to ischemic stroke (1). Cardiovascular involvement is one of the main complications and a major cause of mortality in these patients (3). Herein, we describe a patient with TA presenting with severe acute heart failure secondary to myocarditis.

Case Report

A 38-year-old female patient, previously in good health, reported a history of fatigue, weight loss, and claudication in her left upper limb, accompanied by oppressive chest discomfort that began in 2018. On examination, she presented with a systolic murmur of aortic focus grade III/VI, murmur in the left subclavian artery, radial pulse asymmetry (diminished arterial pulse in her right upper limb), and blood pressure (BP) asymmetry (right upper limb BP 90×60 mmHg and left upper limb BP inaudible). The other physical examination results were unremarkable. Computerized tomography angiography of the thoracic aorta and upper limbs showed occlusion of all branches of the left subclavian artery (Figure 1). The patient was diagnosed with TA based on the 1990 American Rheumatology Association criteria (4). The patient was lost to follow-up, and no therapy was administered. In November 2021, the patient presented with worsening chest pain associated with dyspnea on minimal exertion and was hospitalized for a cardiological investigation. On physical examination, she presented with signs of pulmonary congestion with crackles in her thoracic bases, painful hepatomegaly with hepatojugular reflux, a systolic murmur in aortic focus III/VI, and thread-like pulses with inaudible BP in her left upper limb. Laboratory workup showed normocytic normochromic anemia, renal and hepatic function without abnormalities, increased C-reactive protein levels, and negative serology for hepatitis B and C and human immunodeficiency virus.

An initial cardiac evaluation revealed an elevation of troponin (troponin 5,0 ng/mL, reference <0,5ng/mL) and an electrocardiogram with a left heart block. The transthoracic echocardiogram showed a significant enlargement of the left heart chambers, particularly the left ventricle, which exhibited severe global systolic dysfunction characterized by diffuse hypokinesia. The ejection fraction was measured at 15% using the Teichholz method, and there was a reduction in myocardial strain (-4%). Additionally, there was mild right ventricular dysfunction, and moderate mitral regurgitation of secondary origin, along with mild aortic and tricuspid regurgitation. Pulmonary hypertension was also noted, with an estimated pulmonary artery systolic pressure of 65 mmHg (Figure 2). Cardiac catheterization ruled out ischemic causes. After excluding other etiologies such as prolonged hypertension, coronary artery disease, viral infections, valve diseases, and drug use, acute heart failure was attributed to myocarditis secondary to inflammatory activity. In addition to myocarditis, she also presented myalgia, fatigue, and elevated inflammatory tests (C-reactive protein 10 mg/L, reference <5 mg/L). Despite this, there was no involvement of a new vascular site. An immunosuppressive therapy was instituted. The decision was made to initiate prednisone at a dose of 1 mg/kg and methotrexate at 15 mg/week. After 6 months, a reevaluation showed significant clinical and functional improvements, as shown in Table 1. Cardiac magnetic resonance imaging (MRI), performed 6 months after the introduction of treatment, showed dilated cardiomyopathy with left ventricular dysfunction and absence of typical signs of acute myocarditis (Figure 3).

Discussion

TA is characterized by occlusive vasculitis with a wide clinical spectrum depending on the pattern of the affected vessels. The initial phase has nonspecific inflammatory characteristics and may manifest as fever, fatigue, and weight loss. As the disease progresses, symptoms related to vascular involvement come up (5). Our patient presented with an unusual feature of TA, heart failure

secondary to myocarditis, which was identified by conducting echocardiography with global longitudinal strain. Cardiac involvement is described in up to 60% of TA cases and can affect any cardiac tissue; patients present with various clinicopathological syndromes, including valve dysfunction, coronary arteritis, myocarditis, pericarditis, and even intracavitary cardiac thrombosis (6). The signs and symptoms reflecting this involvement include chest pain, dyspnea, orthopnea, palpitations with heart murmurs, peripheral edema, jugular swelling, pulmonary rales, syncope, and pericardial friction (6).

Myocarditis in TA is generally diagnosed in the early stages of the disease and is accompanied by other features of disease activity. However, this manifestation can occur later in the course of the disease, as observed in the present case. Echocardiography is useful for the initial assessment and may show hypokinesia and left ventricular dilatation (7). Global longitudinal strain (GLS) is an important parameter for evaluating left ventricular function in the echocardiogram, which allows the detection of subclinical systolic dysfunction, despite preserved ejection fraction (8). $GLS \leq -20\%$ is defined as a normal value (9). Another highly useful imaging modality is cardiac MRI, which shows postcontrast enhancement. However, endomyocardial biopsy is the gold standard for diagnosis (7). We were unable to perform the latter procedure on our patient, and an MRI was performed only a few months after the clinical manifestation of heart failure. Takeda *et al.* performed an endomyocardial biopsy of the left ventricle in a young man with TA, whose immunohistochemistry showed infiltration of T lymphocytes with myocyte necrosis, indicating the involvement of cytotoxicity and an active inflammatory process (10).

The pathogenesis of cardiac injury in TA is multifactorial and includes the combination of a chronic inflammatory state with arterial narrowing, arterial hypertension, dyslipidemia with atherosclerosis, and prolonged exposure to corticosteroids (3).

Management of myocarditis in patients with TA is based on immunosuppressive therapy with a satisfactory response (7, 11). Most patients show clinical, structural, and cardiac functional improvement within 2 to 12 weeks of starting immunosuppression (11). Our patient presented clinical and functional improvements following a regimen of prednisone and methotrexate, as revealed in Table 1. This outcome supports our hypothesis that acute heart failure was secondary to myocarditis as a manifestation of TA, even in the absence of an endomyocardial biopsy.

Conclusions

It is important to recognize cardiac involvement in TA, as it has been associated with increased mortality. Early diagnosis and rapid attenuation of inflammation result in better clinical outcomes.

References

1. Kerr GS. Takayasu arteritis. *Ann Intern Med* 1994; 120: 919-29.
2. Chen B, Wang X, Yin W, Gao Y, Hou Z, An Y, et al. Assessment of disease activity in Takayasu arteritis: A quantitative study with computed tomography angiography. *Int J Cardiol* 2019; 289: 144-9.
3. Goel R, Chandan JS, Thayakaran R, Adderley NJ, Nirantharakumar K, Harper L. Cardiovascular and renal morbidity in Takayasu arteritis: a population-based retrospective cohort study from the United Kingdom. *Arthritis Rheumatol* 2021; 73: 504-11.
4. Arend WP, Michel BA, Bloch DA, Hunder GG, Calabrese LH, Edworthy SM, et al. The American College of Rheumatology 1990 criteria for the classification of takayasu arteritis. *Arthritis Rheum* 2010; 33: 1129-34.
5. Kim H, Barra L. Ischemic complications in Takayasu's arteritis: a meta-analysis. *Semin Arthritis Rheum* 2018; 47: 900-6.
6. Miloslavsky E, Unizony S. The heart in vasculitis. *Rheum Dis Clin North Am* 2014; 40: 11-26.
7. Talwar KK, Kumar K, Chopra P, Sharma S, Shrivastava S, Wasir HS, et al. Cardiac involvement in nonspecific aortoarteritis (Takayasu's arteritis). *Am Heart J* 1991; 122: 1666-70.
8. Kalam K, Otahal P, Marwick TH. Prognostic implications of global LV dysfunction: a systematic review and meta-analysis of global longitudinal strain and ejection fraction. *Heart* 2014; 100: 1673-80.
9. Voigt JU, Pedrizzetti G, Lysyansky P, Marwick TH, Houle H, Baumann R, et al. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *Eur Heart J Cardiovasc Imaging* 2015; 16: 1-11.
10. Takeda N, Takahashi T, Seko Y, Maemura K, Nakasone H, Sakamoto K, et al. Takayasu myocarditis mediated by cytotoxic T lymphocytes. *Intern Med* 2005;44:256-60.
11. An X, Han Y, Zhang B, Qiao L, Zhao Y, Guo X, et al. Takayasu arteritis presented with acute heart failure: case report and review of literature. *ESC Heart Fail* 2017; 4: 649-54.

Table 1. Evolution of cardiac parameters during treatment.

	Initial echocardiogram	Echocardiogram after 6 months of treatment
Ejection fraction	15% (Teichholz)	34% (Teichholz)
Global longitudinal strain (reference GLS \leq -20%)	-4%	-12%
Functional Class (NYHA)	Initial NYHA	NYHA after 6 months of treatment
	NYHA IV	NYHA II
Troponin (reference <0.5 ng/dL)	Initial troponin	Troponin after 6 months of treatment
	5.0 ng/dL	0.003 ng/dL

GLS, global longitudinal strain; NYHA, New York Heart Association.



Figure 1. Computerized tomography angiography of the thoracic aorta 3d: occlusion of the left subclavian artery.

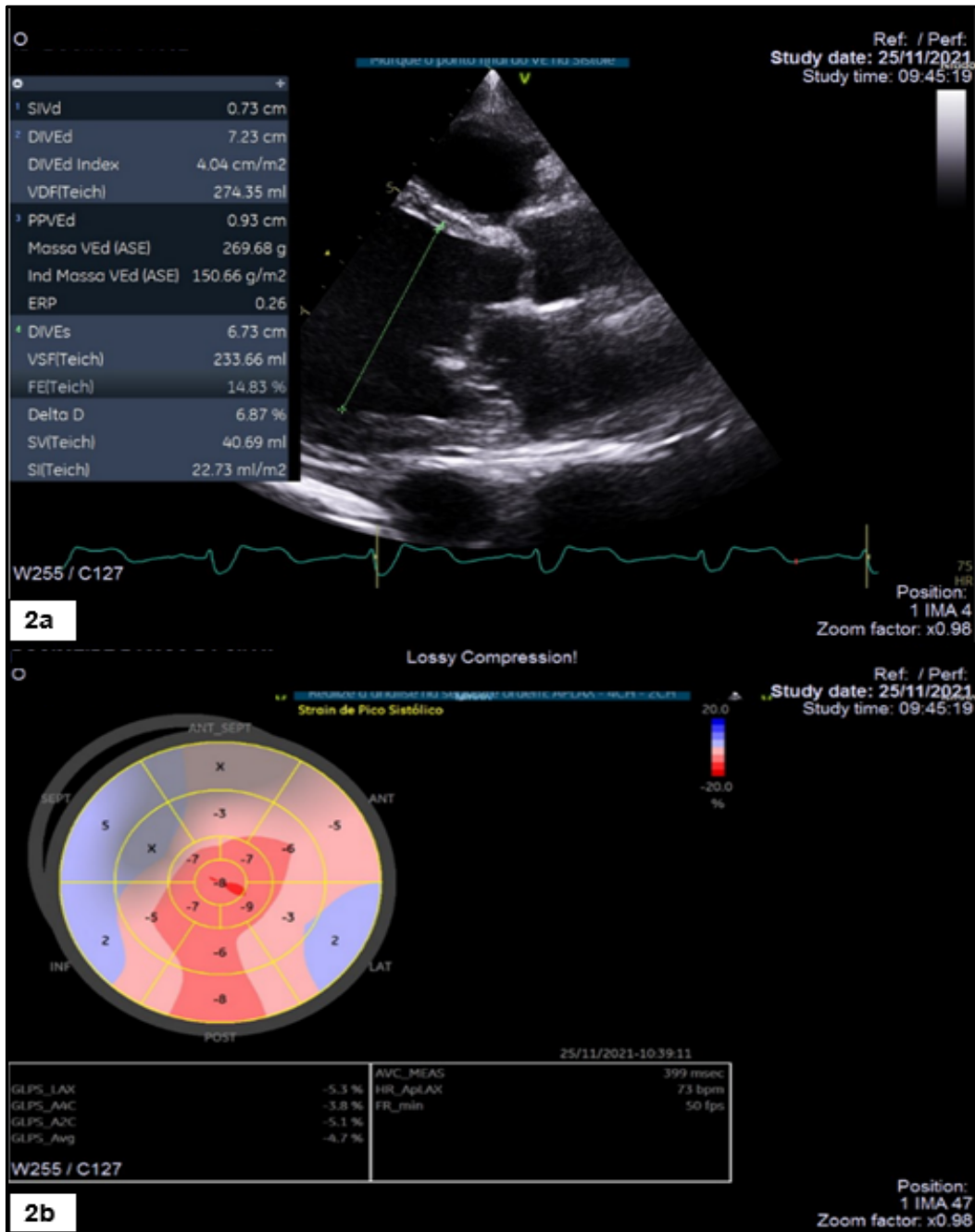


Figure 2. Echocardiogram. A) Severe global systolic dysfunction; B) reduced myocardial strain (-4%) showing myocardial injury.

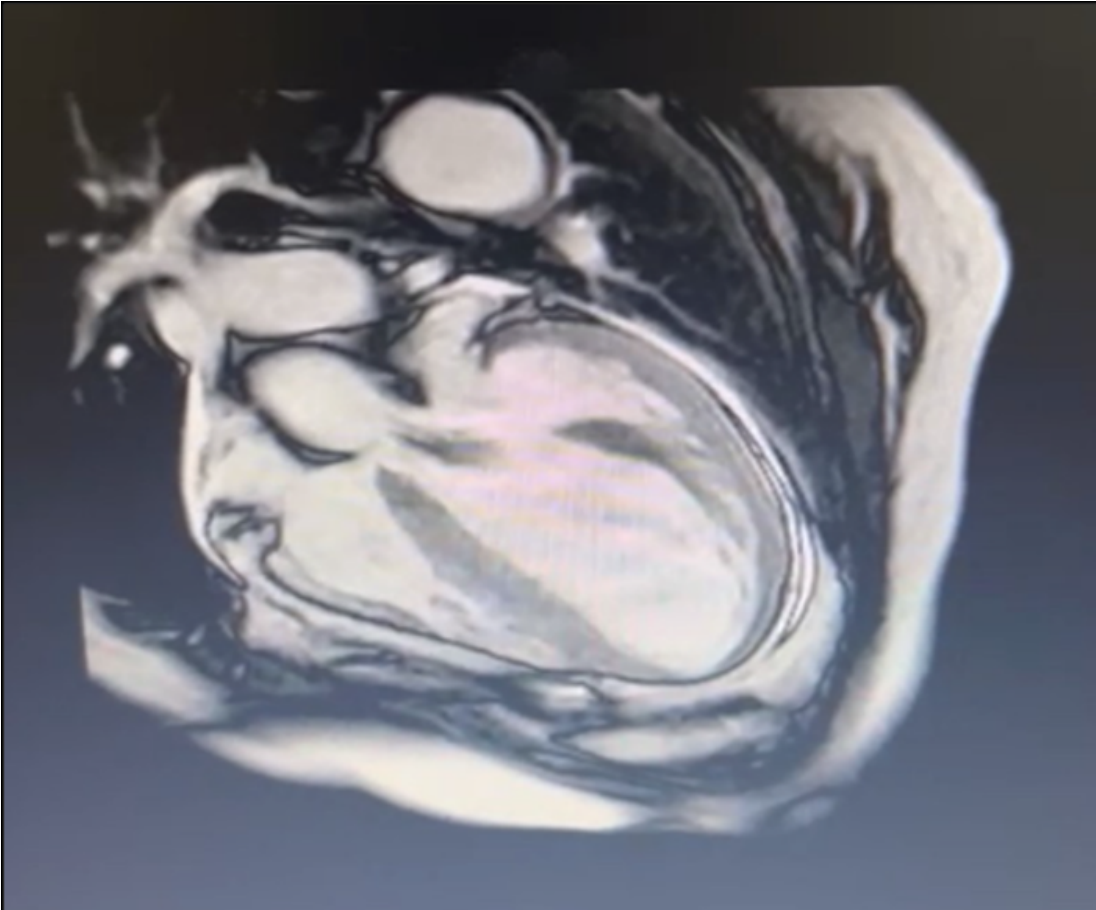


Figure 3. Cardiac magnetic resonance imaging: dilated cardiomyopathy with left ventricular dysfunction.